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Method and apparatus for obtaining human or animal samples for analytics and diagnostics

The invention pertains to the field of medical analysis and diagnosis. It relates, in particular, to a method and an apparatus for obtaining samples from air exhaled by human or animal subjects.

Not only in the current situation is there a great need for simple, safe, fast, painless and non-invasive procedures for obtaining samples from human or animal subjects for chemical or biological, in particular medical analysis and/or diagnostics, which procedures, if possible, may also be carried out by persons without profound nursing or even medical training, especially by the human subjects themselves; as well as for devices that allow for the respective procedures to be carried out conveniently, ideally in a simplified manner, inhibit incorrect performance, and/or allow for simple and efficient quality control measures to be put in place.

For a subsequent examination of the samples a wide range of well-known methods is available. In particular, it should be possible to use mass spectroscopic or PCR (polymerase chain reaction) based analysis methods. The subsequent examination may, in particular, aim at detecting a presence or confirming an absence of specific biomarkers in the obtained samples.

A biomarker as referred to and to be understood hereinafter may be a pathogen, and may in particular comprise a virus, bacteria, fungus or fraction thereof, in particular genetic material characteristic of said virus, bacteria, or fungus. A biomarker may in particular, comprise a fraction of a DNA or RNA characteristic of said pathogen, virus, bacteria, or fungus. A biomarker may in particular comprise a substance, in particular an antigen, a metabolic product, specifically indicative of a presence of a particular virus, bacteria, fungus or fraction thereof, in particular produced by a metabolism of said virus, bacteria, or fungus. The above biomarkers may be thought of as direct biomarkers, characterized in that they directly or indirectly cause a (undesired) condition or disease.

A biomarker may also comprise a substance adapted to specifically bind to a particular pathogen, virus, bacteria, fungus or fraction thereof, in particular an antigen, genetic material characteristic of said pathogen, virus, bacteria, or fungus, and preferably to at least not significantly bind to any other pathogen, virus, bacteria, fungus or fraction thereof; or a substance adapted to specifically bind to a substance, in particular a metabolic product, specifically indicative of a presence of a particular pathogen, virus, bacteria, fungus or fraction thereof. The latter class

of biomarkers thought of as indirect biomarkers, which may in particular comprise substances which facilitate a detection, discrimination, quantization etc. of direct biomarkers which may be more difficult to detect, discriminate, and/or quantize directly. An antibody is a further example of what may be considered an indirect biomarker.

Therefore, it would be desirable to be able to obtain samples from and/or biomarkers contained in human or animal respiration in a simple, safe, fast, painless and non-invasive manner.

SUMMARY OF THE INVENTION

The above objective and other objectives are solved by a method and an apparatus in accordance with the independent claims. Preferred embodiments and/or variations of the invention are presented in dependent claims.

A method for detecting biomarkers in human or animal respiration in accordance with an aspect of the invention as hereinafter claimed comprises the steps of claim 1 below.

A method for detecting biomarkers, in particular a presence of biomarkers, in air exhaled by a human or animal subject in accordance with the invention may comprise the steps of

a. sampling air exhaled by the subject to obtain a sample, in particular by liquifying humidity contained in the exhaled air;
b. subjecting the sample to biochemical analysis, in particular PCR (polymerase chain reaction), mass spectroscopy, chromatography, or magnetic resonance spectroscopy to detect a presence or absence of biomarkers in the exhaled air.

To - at least potentially - increase an amount and/or concentration of biomarkers in the exhaled air, the subject may be stimulated to temporarily adapt and/or modify breathing, in particular to temporarily adapt and/or modify an inhalation and/or exhalation depth, frequency, rate and/or speed.

At least for human subjects, such stimulation may include a feedback signal which is provided to the subject, and which is obtained by observing and/or monitoring respiration of the subject.

For animal subjects, substantial training may be required for stimulation to temporarily adapt and/or modify breathing to become effective.

An assisting person or a health care professional may be required to and/or may support the subject, and/or supervise the examination, in particular the sampling and/or collecting of exhaled air, in particular for animal subjects.

The stimulation, in particular the feedback, may be employed to signal and/or aimed at signaling the subject to perform a particular breathing sequence, which may in particular comprise two or three breaths carried out in a specific manner that will maximize or at least increase an amount and/or concentration of biomarkers in the air exhaled after the two breaths, and/or in the third breath.

Said particular breathing sequence may start with a deep exhalation, wherein the subject may be stimulated, e.g. by an exhale signal, to and/or tries to exhale as deeply as possible, thus minimizing an amount of air that remains in the subject's lungs. After said exhalation, the subject may stimulated, e.g. by an inhale signal, and/or try to inhale as quickly and/or strongly as possible. The quick and/or strong inhalation will lead to a significant, momentary negative pressure in the lungs of the subject. Said negative pressure will give rise to an enhanced release of substances from lung mucosa, in a form comprising droplets, aerosol and evaporation products, which may in turn comprise one or more biomarkers.

The substances thus released will subsequently be exhaled by the subject, in particular with the next exhalation, but also, possibly to a lesser degree, in subsequent exhalations.

The air exhaled may be collected and cooled to liquify humidity contained therein, in particular by condensation, thus forming a condensate. The condensate or a or portion thereof may be used as a sample and subsequently be subjected to chemical or biological analysis, which may comprise or be followed by, medical analysis and/or diagnostics. In particular, the condensate or a sample thereof may be subjected to PCR analysis, chromatography and/or mass spectroscopy. The condensate or a sample thereof may also be subjected to optical analysis including microscopy, image processing, cytometry, etc. The chemical or biological analysis, and or a subsequent medical analysis and/or diagnostics, may or may need to be carried out at a remote location, in particular at a dedicated laboratory or facility.

The method may comprise the step of monitoring respiration of the subject over a period of time, in particular a period of time immediately preceding the sampling of exhaled air. The period of time may extend over a plurality of breaths, and/or, in particular, about a time span of between some ten seconds and a few minutes. To allow for efficient monitoring, means for measuring respiratory flow may be employed. In particular, the subject may be required to breathe through a conduit, in particular a tube, hose or pipe, which may comprise a flowmeter or gas flow sensor configured to measure, in particular, a flow rate and direction within and/or through the conduit. The monitoring may thus in particular comprise measuring a respiratory flow, in particular a flow rate and direction as a function of time.

The monitoring may aim at estimating and/or analyzing lung volumes and/or pulmonary function of the subject, in particular at estimating parameters indicative of pulmonary function. In particular, a forced vital capacity, FVC, and/or a maximum inspiratory flow or peak inspiratory flow, PIF, achievable by the subject may be estimated on the basis of the monitoring. The estimation may take into account external information related to the subject, which may comprise a medical anamnesis and/or observables like age, size, weight and/or gender of the subject, e.g. by forming a (weighted) average between first parameters determined and/or estimated exclusively on the basis of the monitoring, and corresponding second parameters determined from said external information. External information may also comprise and/or be enhanced by statistic information, in particular related to public health.

During the monitoring, one or more signals, in particular feedback signals, may be provided to the subject, said signals indicative of whether the subject is supposed to inhale, exhale or (temporarily) hold its breath. The signals, in particular feedback signals, may further provide an indication of how fast and/or strong the subject is expected to exhale or inhale.

Lung volumes and/or parameters indicative of pulmonary function of the subject may then be estimated from the flow measurements, and/or a correlation or other correspondence between the one or more signals , in particular feedback signals, provided to the subject and respiratory flow measured over time and/or in response to the various signals, in particular feedback signals. The corresponding estimation may further comprise statistical analysis based on repeatedly providing an identical signal or several different signals, in particular feedback signals, to the subject, measuring the corresponding respiratory flow, and estimating average values, standard deviations, confidence intervals etc. for the estimated lung volumes or estimated parameters indicative of pulmonary function, in particular estimated FVC or PIF.

The estimated lung volumes and/or parameters indicative of pulmonary function may be used to determine and/or verify whether/that the subject did at least approximately fully exhale, and/or did at least approximately inhale as quickly and/or strongly as possible during the particular breathing sequence as detailed further above. Only if or when this is the case, the air exhaled by the subject may be collected and/or sampled, in particular be cooled to liquify humidity contained therein, thus forming a condensate to obtain the sample.

If, on the other hand, it is determined that the subject did not at least approximately fully exhale, and/or did not at least approximately inhale as quickly and/or strongly as possible during the particular breathing sequence as detailed further above, monitoring the respiration of the subject may be continue, and/or the respective period of time extended, without air exhaled by the subject being collected and/or sampled, in particular without exhaled air being cooled to liquify humidity contained therein. A feedback signal indicative of that the subject is required to continue breathing normally may be provided to the subject. After some time, e.g. between 30 seconds and three minutes has elapsed, the sequence may begin again with the subject being stimulated to and/or trying to exhale as deeply as possible, as described above.

Data obtained by measuring respiratory flow, which may comprise respiratory flow rate and/or direction a function of time, and which may be obtained in particular during the particular breathing sequence as detailed above, but also during monitoring, may be recorded and/or stored in a memory, in particular to allow for subsequent verification, in particular quality control of the sample, wherein an amount of deviation from full exhalation and/or from PIF may be (inversely) related to sample quality.

Instead of trying to stimulate the subject to adapt and/or modify his/her/its breathing, exhaled air may also be sampled, in particular collected, over a number of, preferably consecutive, exhalations. To increase an amount and/or concentration of biomarkers in the exhaled air, a breathing frequency and /or depth may be increased other than be (conscious) stimulation, e.g. by subjecting the subject to physical exercise prior to sampling/collecting exhaled air.

An apparatus for obtaining a sample from a human or animal subject in accordance with an aspect of the invention as hereinafter claimed comprises the features of claim 8 below.

An apparatus for obtaining a sample from a human or animal subject in accordance with the invention may comprise

a. a first conduit for receiving air exhaled by the subject;

b. a first flowmeter provided in the first conduit;

c. a condensation vessel;

d. cooling means for cooling the condensation vessel;

e. a closure for closing, and preferably hermetically sealing, the condensation vessel;

f. valve means (4) provided in, in particular fluidly connected with, the first conduit configured to selectively

i. channel exhaled air into the condensation vessel and out of the condensation vessel into an environment, or

ii. channel exhaled air into an environment without the air passing through the condensation vessel.

The apparatus may, in particular, be used when carrying out the method as described above. To monitor respiration of the subject over a period of time, the subject may or may be brought to exhale through the first conduit over a period of time, in particular over a number of breaths each comprising an inhalation and an exhalation. The first conduit may thus comprise an at least essentially tubular section at a first or proximal end thereof, which may be formed integrally or detachably with the first conduit. A subject, in particular a human subject, may place a first or proximal end of the essentially tubular section in his/her mouth, enclose it tightly with his her lips, and exhale by blowing through the through the essentially tubular section and the first conduit. Alternatively, a mask may be a first or proximal end of the first conduct, which may be placed over the subject's mouth, and which may optionally also cover the subject's nose.

A first flowmeter provided in the first conduit may measure, in particular, a flow rate and direction of fluid, in particular exhaled air, within and/or through the first conduit.

A port may be provided in the first conduit, at or to which the condensation vessel may be connected. Valve means, in particular a first valve, may be provided and configured to, in a first position, direct air exhaled by the subject past the condensation vessel and into an environment of the apparatus and/or the subject. When the valve means, in particular the first valve, is in a second position different from the first position, air exhaled by the subject may be channeled from the first conduit into the condensation vessel, and from the condensation vessel into an environment, either directly or through a section of the first conduit

downstream of the valve means, in particular the first valve. With the valve means in the second position, air exhaled by the subject is thus - at least temporarily - collected, in particular to obtain a sample.

Cooling means may allow for cooling the condensation vessel, in particular a wall of the condensation vessel. Humidity contained in the air exhaled by the subject will thus condensate to form the sample, which will aggregate and/or be collected in the condensation vessel.

The apparatus may comprise a second conduit through which the subject may inhale. The second conduit may branch off the first conduit in an area between the valve means and the essentially tubular section or the mask. Further valve means, in particular a second and (optional) third valve may be present in the first and/or second conduit, respectively, to ensure that air inhaled or aspired by the subject does not pass through the valve means, in particular not through the first valve and/or does not pass by the port provided in the first conduit. A second flowmeter may be provided in the second conduit to measure, in particular, a second flow rate and a second direction of fluid, in particular inhaled air, within and/or through the second conduit.

An area around the port of wall or material surrounding and/or defining the first conduit may act as and/or form a closure for the condensation vessel which may hermetically seal the condensation vessel, in particular when the valve means, in particular the first valve, is in its first position.

If no second conduit is provided, the subject may inhale by aspiring air through the first conduit.

The valve means and further valve means may be configured to be actuated manually. When air exhaled by the subject is to be collected as described above, a feedback signal indicative of that the valve needs to be actuated, in particular put into the second position, may be provided to the subject, an assisting person or a health care professional. At other times, in particular when air exhaled by the subject is not to be collected, a feedback signal indicative of that the valve needs to be (put) in(to) the first position may be provided. Additionally or alternatively, the valve means and further valve means may be configured to be actuated by one or more actuators comprised by the apparatus, in particular under control of the electronic circuitry. The apparatus may comprise a position sensor for detecting and/or monitoring a

condition and/or setting of the valve means, in particular of the first valve. A sensor signal indicative of said condition and/or setting may thus be obtained.

The apparatus may comprise electronic circuitry, which may be configured to control any sensing means comprised by the apparatus, in particular the flowmeter or flowmeters. The electronic circuitry may, in particular, switch between various operation modes of the sensing means, which operation modes may comprise an active and an inactive, stand-by or power-saving mode.

The electronic circuitry may be configured to receive sensor signals generated by the sensing means. The electronic circuitry may be configured to verify, process or pre-process the received signals. The electronic circuitry may be configured to forward the received signals, in particular transfer the received signals to an external unit, in particular to a computing device, which computing device may be configured to analyse the signal; and/or to generate a feedback command, in particular represented by an electric signal, or a feedback signal for providing feedback to the subject or an assisting person or a health care professional.

The electronic circuitry may comprise or represent a logic circuit. The electronic circuitry may comprise an integrated circuit, in particular a general purpose central processing unit (CPU), a graphics processing unit (GPU), a microcontroller, a reduced instruction set computer (RISC) processor, an application specific integrated circuit (ASIC), a programmable logic circuit (PLC), a field programmable gate array (FPGA), a digital signal processing (DSP) device, and/or any other circuit or processing device capable of providing and/or executing functionalities described above and/or below, in particular controlling of the excitation means and the sensing means.

The apparatus may comprise stimulation means for rendering the feedback signal perceivable to the subject, in particular for converting the feedback command into a signal perceivable to the subject. The stimulation means may comprise display means, in particular LEDs or a dot-matrix display, capable of displaying different patterns, colors, images etc. to provide an optical feedback signal in dependence on the feedback command. Additionally or alternatively, the stimulation means may comprise acoustic and/or haptic feedback means for providing acoustic and/or haptic feedback signals in dependence on the feedback command.

The apparatus may further comprise and human interface (HID) device for allowing the subject and/or an assisting person or a health care professional to interact with the electronic circuitry. The HID may, in particular, comprise a plurality of buttons, which may be arranged as a keyboard, and which may be connected with the electronic circuitry such that the latter may detect whether one or more buttons are pressed or not. Additionally or alternatively, the HID may

comprise a touchscreen, which may also serve as display means. The HID may thus allow for entering data, commands, settings etc, which may be stored and/or processed by the electronic circuitry, and may change a configuration and/or behaviour of the electronic system.

The electronic circuitry may comprise communication means for communicating with an external unit, in particular with a computing device, to transmit and/or receive data and/or commands, in particular to transmit the signals as provided by the sensing means to said external unit. The communication means may be configured to communicate using wireless communication techniques, in particular Bluetooth™, wireless network (e.g. WLAN) or cellular phone communication technologies, and may be adapted to communicate over local area (LAN) and/or wide area (WAN) networks.

The apparatus may comprise a power source, in particular an electric power source, for powering the electric circuit, sensor(s), actuator(s), etc. The power source may comprise a (rechargeable) battery.

A **respiratory biomarker sampling system** in accordance with a further aspect of the invention may comprise an apparatus for obtaining a sample as described above and a control unit, and/or may be configured to be used to execute and/or support execution of the method in accordance with the invention as described further above.

The control unit may be configured to control any sensing means, actuators, stimulation means, HIDs, and/or communication means comprised by the apparatus. The control unit may be configured to verify, process, analyze, store and/or forward any sensor signals received from the sensing means, in particular to estimate parameters indicative of pulmonary function as, e.g., a forced vital capacity, FVC, and/or a maximum inspiratory flow or peak inspiratory flow, PIF, achievable by the subject. The control unit may be configured to generate the one or more feedback commands or feedback signals which may be provided to the stimulation means and/or the subject as described above for the method in accordance with the invention, and/or the control stimulation means to provide according feedback to the subject. The control unit may be configured to receive an input from the subject through the HID.

The control unit may be integrated with and/or comprised by the electronic circuitry of the apparatus for obtaining a sample as described above.

Alternatively, the control unit may be implemented as or on an external unit separate from the apparatus for obtaining a sample as described above, and be connected to the electronic circuitry through the communication means of the apparatus as described above.

In particular, a computing device, e.g. a computer, smartphone, handheld computation device (also referred to as tablet computer) or the like, capable of communicating with the electronic circuitry through the communication device may serve as the control unit, wherein the computer, smartphone, handheld computation device, or the like, may execute a computer program, in particular an application (also referred to as an "app") comprising instructions which cause the control unit thus constituted to execute some or all steps of the method as described above, or as claimed below.

The control unit may comprise a memory, and may be configured to store sensor signals received from the sensing means, parameters indicative of pulmonary function, in particular as determined from said sensor signals, and/or feedback commands or feedback signals.

When the control unit is realized as an external unit, in particular by or on a computing device, the stimulation means and/or the HID may also be provided by or as part of the external unit.

The apparatus for obtaining a sample and/or the external unit as described above may comprise a camera or a scanner, in particular a bar code or QR code scanner, capable of identifying a unique tag on a sample storage and/or transport means, in particular a sample storage vial. The unique tag may be a multi-digit number or alphanumeric code, comprising in particular more than 4, 5, 6 or 10 digits, wherein a different unique tag may be applied to each individual sample storage and/or transport means supplied or produced by a producer and/or supplier, respectively, or by a group of suppliers or producers. When, in particular prior to, obtaining a sample as in the method described above, the subject, an assisting person or a health care professional may scan the tag with the camera or the scanner. The tag and/or a representation thereof may then be stored in the memory of the control unit.

The tag and/or a representation thereof may be transmitted to a dedicated laboratory or facility capable of carrying out the chemical or biological analysis, and or the subsequent medical analysis and/or diagnostics the sample is to be subjected, together with any other data obtained when the sample was obtained, in particular sensor signals and/or measurements obtained during the monitoring and/or parameters indicative of pulmonary function determined

on the basis of such signal sensor signals and/or measurements. Transmission of tag and/or data may be handled by the communication means of the electronic circuitry, or by communication, in particular networking, capabilities of the control unit, in particular computing device, which may for data communication over LAN and or WAN and/or using Ethernet, Bluetooth™, wireless network (e.g. WLAN), and/or cellular network according to standards like, in particular 3G, 4G or 5G, or any future standards yet to be developed.

A sample collection unit for collecting, handling and storing a sample obtained from a human or animal subject in accordance with an aspect of the invention as hereinafter claimed comprises the features of claim 16 below.

BRIEF DESCRIPTION OF THE DRAWINGS

The subject matter of the invention will be explained with respect to further optional detail in the following text with reference to further exemplary embodiments which are illustrated in the attached drawings.

Fig 1 shows an exemplary apparatus for obtaining a sample from a human or animal subject, in accordance with the invention as hereinafter claimed.

Fig 2 shows an exemplary sample collection unit for collecting, handling and storing a sample obtained from a human or animal subject, in accordance with the invention as hereinafter claimed.

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

The apparatus for obtaining a sample shown in Fig. 1 comprises a first conduit 10 which may receive air exhaled by a subject, which is divided into a first portion and a second portion by a valve 4, said second portion located downstream of the first portion. A first pressure sensor 101a is provided in the first portion of the first conduit 10; and a second pressure sensor 101b is provided in the second portion of the first conduit 10. The first and second pressure sensors 101a, 101b are configured to measure first and second pressures in the first and second portion of the first conduit 10.

The apparatus further comprises a receptacle 2 for a condensation vessel 3, in which humidity contained in the air exhaled by the subject may be liquified. The receptacle may contain cooling means, e.g. a thermoelectric cooler or Peltier device, which allow to cool the condensation vessel 3, in particular the walls of the condensation vessel 3, preferably to a temperature around 0°C, in particular between -5,0°C and +5,0°C. The condensation vessel 3 comprises an opening at an upper thereof, an elongate middle section 31, which is at least essentially circular and/or has an at least essentially circular inner cross section, and an at least approximately conical lower part 32.

The apparatus further comprises a closure 1, which may be used to close and hermetically seal the condensation vessel 3. In the exemplary embodiment of Fig. 1, the first conduit 10 is formed integrally with the closure 1, and the valve 4 and the first and second pressure sensors 101a, 101b are provided in the closure 1. The valve 4 comprises a piston 41 which can be moved between a first position shown in Fig. 1a), and a second position in shown in Fig. 1b). A spring 42 is provided to preset the piston 41 in the first position, from which it may be moved into the second position by pressing a button 43 provided on one side of the piston towards the closure.

In the first position, a bypass conduit provided in the piston or between the piston and the first conduit fluidly connects the first portion and the second portion of the first conduit 10. At the same time, the piston 41 and the closure jointly seal the condensation vessel 3.

In the second position, a connection conduit fluidly connects the first portion of the first conduit 10 with the condensation vessel 3, and the condensation vessel 3 with the second portion of the first conduit 10.

The apparatus may further comprise a position sensor (not shown in Figs 1a and 1b), which may monitor the position of the valve 4, in particular of the piston 41, and may generate a signal indicative of said position, in particular of whether the piston is in the first position or in the second position.

The first and second pressure sensors 101a, 101b allow for quantifying a flow of exhaled or aspired air in and/or through the first conduit 10, in particular by applying Bernoulli's principle. A flow rate and/or flow direction of air in the first conduit 10 may then be calculated and/or otherwise determined from and/or on the basis of pressure measurements from both of the sensors.

Fig. 2 shows an exemplary sample collection unit for collecting, handling and storing a sample obtained from a human or animal subject, in accordance with the invention as hereinafter claimed, in particular by using the apparatus from claim 1.

The sample collection unit comprises a condensation vessel 3, a plunger 6 and a sample storage vial 8. The plunger comprises a funnel in form of an at least essentially funnel-shaped washer 61 provided on a first or distal end of the plunger 6. The plunger 6, in particular the funnel-shaped washer 61, may be inserted into the condensation vessel 3 through opening 30, which may be formed on a first end of the condensation vessel, in particular with a filler opening of the funnel first and/or ahead. Shape and/or dimensions of an outer circumference of the funnel, in particular an outer circumference of a filler opening of the funnel, in particular of funnel-shaped washer 61 are selected to at least essentially match an inner cross section of the elongate middle section 31 of the condensation vessel 3. The filler opening of the funnel or funnel shaped washer 61 may, in particular, correspond to a larger opening of said funnel or funnel shaped washer 61.

The funnel-shaped washer 61 or at least the circumference thereof is preferably made out of a soft and/or flexible material, preferably an elastomer like silicone, rubber or the like. As the plunger 6 is advanced into the condensation vessel 3, in particular towards or in a direction of second end of the condensation vessel remote from and/or opposite the first end, a circumference, in particular an outer circumference of the funnel-shaped washer 61 successively wipes an inner surface 311 of the elongate middle section 31, thereby directing and/or forcing any condensate formed on said inner surface towards the conical lower part 32 of the condensation vessel 3, where said condensate will accumulate.

The plunger may, in particular, be advanced by pushing onto a second or proximal end 62 thereof. A channel 63 is provided inside the plunger 6 and fluidly connected to a collection volume 611 of the funnel formed by the funnel-shaped washer 61 at a first end of the channel 63. A sample storage vial 8 may be fluidly connected to a second end of the channel 63. As illustrated in Figures 2 c) and d), a recess 64 may be foreseen in the second or proximal end 62 of the plunger 6, which recess 64 may be sized and/or shaped to accommodate at least a portion of the sample storage vial 8 near an opening 81 of said sample storage vial 8. When the sample storage vial 8 is placed into the recess 64 as foreseen, the second end of the channel 63 extends into and/or partially through the opening 81. When the thus assembled sample collection unit is turned upside down, such that the opening 81 of the sample storage

vial 8 faces upwards and the opening 30 of the condensation vessel 3 faces downwards, condensate that has accumulated in the conical lower part 32 will flow in a downward, be collected by the funnel-shaped washer 61, and flow into sample storage vial 8 through channel 63.

The condensation vessel 3 with the inserted plunger 6 may then be removed from sample storage vial 8 by moving them in relatively opposite directions, wherein the sample storage vial 8 may remain in an upright position, i.e. with the opening 81 of said sample storage vial 8 facing upwards.

The sample storage vial 8 may then be closed in a fluid- and/or gas-tight manner to allow for the sample to be safely and securely transported to an analysis equipment or facility. This may be achieved by a cap that me be screwed, press-fit or the like onto or into the opening 81. Alternatively, the sample storage vial 8 may comprise a septum, in particular made out of silicone and/or PTFE, which may be penetrated by an appropriately adapted, in particular pointed and/or edged second end of the channel 63, when the sample storage vial 8 is inserted into the recess 64; and which will automatically seal the opening when the sample storage vial 8 is separated from the condensation vessel 3 with the inserted plunger 6.

A unique tag may be provided on an outside of the sample storage vial 8, and may in particular printed onto or engraved into an outside wall of the sample storage vial 8. The tag may also be printed onto a sticker which may be firmly attached to the sample storage vial 8.

This description and any accompanying drawings that illustrate aspects and embodiments of the present invention should not be taken as limiting the claims defining the protected invention. In other words, while the invention has been illustrated and described in detail in the drawings and foregoing description, such illustration and description are to be considered illustrative or exemplary and not restrictive. Various mechanical, compositional, structural, electrical, and operational changes may be made without departing from the spirit and scope of this description and the claims. In some instances, well-known circuits, structures and techniques have not been shown in detail in order not to obscure the invention. Thus, it will be understood that changes and modifications may be made by those of ordinary skill within the scope and spirit of the following claims. In particular, the present invention covers further embodiments with any combination of features from different and/or individual embodiments

as described above and below. Embodiments in accordance with the invention may, in particular, include further and/or additional features, elements, aspects, etc. not shown in the drawings or described above.

The disclosure also covers all further features shown in any Figure, individually, although they may not have been described in the afore or following description. Also, individual alternatives of the embodiments described in any Figure and the description and individual alternatives of features thereof can be disclaimed from the subject matter of the invention or from disclosed subject matter. The disclosure comprises subject matter consisting of the features defined in the claims or the exemplary embodiments as well as subject matter comprising said features.

The present disclosure also includes embodiments with any combination of features which are mentioned or shown above and/or below, in various embodiments or variants. It also includes individual features as shown in the Figures, even if they are shown there in connection with other features and/or are not mentioned above or below. The disclosure comprises embodiments which exclusively comprise the features described in the claims or the exemplary embodiments, as well as those which comprise additional other features. The steps of any method disclosed above or claimed below may preferably be carried out according the order in which they are presented, but may also be carried out in a different order.

Furthermore, in the claims the word "comprising" does not exclude other elements or steps, and the indefinite article "a" or "an" does not exclude a plurality. A single unit or step may fulfil the functions of several features recited in the claims. The mere fact that certain measures are recited in mutually different dependent claims does not indicate that a combination of these measures cannot be used to advantage. The terms "essentially", “substantially”, "about", "approximately" and the like in connection with an attribute or a value particularly also define exactly the attribute or exactly the value, respectively. The term "about" in the context of a given numerate value or range refers to a value or range that is, e.g., within 20%, within 10%, within 5%, or within 2% of the given value or range. Components described as coupled or connected may be electrically or mechanically directly coupled, or they may be indirectly coupled via one or more intermediate components. Any reference signs in the claims should not be construed as limiting the scope.

Embodiments of the invention may involve one or more electronic or computing devices, and/or involve the use of such devices. Said devices typically include a processor, processing device,

or controller, such as a general purpose central processing unit (CPU), a graphics processing unit (GPU), a microcontroller, a reduced instruction set computer (RISC) processor, an application specific integrated circuit (ASIC), a programmable logic circuit (PLC), a field programmable gate array (FPGA), a digital signal processing (DSP) device, and/or any other circuit or processing device capable of executing the functions described herein. In particular, the battery management system, the control system may, and/or the control system settings update unit may be partially or fully implemented on such electronic or computing devices, individually or jointly.

The methods described herein may be partially or fully implemented as or in the form of software, which may in turn be encoded as executable instructions embodied in a non-transitory computer readable medium, including, without limitation, a storage device and/or a memory device. Such instructions, when executed by a processing device, cause the processing device to perform at least a portion of the methods described herein, preferably in real-time. The above examples are exemplary only, and thus are not intended to limit in any way the definition and/or meaning of the term processor and processing device.

As used herein, i.e. anywhere in this document, the terms “computer”, "computing device", "smartphone", and related terms, e.g., “processor”, “processing device,” central processing unit (CPU)”, “controller” and/or "control unit" may not be limited to just those integrated circuits referred to in the art as a computer, but broadly refers to a microcontroller, a microcomputer, a programmable logic controller (PLC), and application specific integrated circuit, and other programmable circuits, and these terms are used interchangeably herein. In the embodiments described herein, memory may include, but is not limited to, a computer-readable medium, such as a random access memory (RAM), a computer-readable non-volatile medium, such as a flash memory. Alternatively, a floppy disk, a compact disc – read only memory (CD-ROM), a magneto-optical disk (MOD), a digital versatile disc (DVD), a USB stick and/or a flash memory card (e.g. CF, SD, miniSD, microSD) may also be used. Also, in the embodiments described herein, additional input channels may be, but are not limited to, computer peripherals associated with an operator interface such as a mouse and a keyboard. Alternatively, other computer peripherals may also be used that may include, for example, but not be limited to, a scanner. Furthermore, in the exemplary embodiment, additional output channels may include, but not be limited to, an operator interface monitor.

Further, as used herein, the terms “software” and “firmware” are interchangeable and include any computer program which may be stored in memory for execution by computers as defined above, workstations, clients, and/or servers.

As used herein, the terms “non-transitory computer-readable media”, "computer-readable non-volatile medium", etc. are intended to be representative of any tangible computer-based device implemented in any method of technology for short-term and/or long-term storage of information, such as, computer-readable instructions, data structures, program modules and sub-modules, or other data in any device. Therefore, the methods described herein may be encoded as executable instructions embodied in a tangible, non-transitory, computer-readable medium, including, without limitation, a storage device and/or a memory device. Such instructions, when executed by a computer as defined above, cause the computer to perform at least a portion of the methods described herein. Moreover, as used herein, the term “non-transitory computer-readable media” may include all tangible, computer-readable media, including, without limitation, non-transitory computer storage devices, including without limitation, volatile and non-volatile media, and removable and non-removable media such as firmware, physical and virtual storage, CD-ROMS, DVDs, and any other digital source such as a network or the Internet, as well as yet to be developed digital means, with the sole exception being transitory, propagating signal.

Patent claims

1. A method for detecting biomarkers in air exhaled by a human or animal subject, the method comprising the steps of
    a. sampling, in particular collecting, air exhaled by the subject to obtain a sample;
    b. subjecting the sample to biochemical analysis, in particular PCR (polymerase chain reaction), mass spectroscopy, chromatography, or magnetic resonance spectroscopy to detect a presence or absence of biomarkers in the exhaled air.

2. The method of claim 1, further comprising the steps of
    a. monitoring respiration of the subject over a period of time;
    b. providing a feedback signal to the subject, in particular a feedback signal indicative of how to adapt breathing to increase an amount of biomarkers in the exhaled air, in particular by adapting an inhalation and/or exhalation depth, frequency, rate and/or speed.

3. The method of claim 1 or claim 2, further comprising the steps of
    a. cooling the exhaled air to liquify humidity contained therein, thus forming a condensate,
    b. sampling the condensate to obtain the sample.

4. The method of claim 2 or claim 3, wherein monitoring respiration of the subject comprises
    a. estimating lung volumes, in particular a forced vital capacity, FVC, of the subject; and/or
    b. estimating a maximum inhalation rate, in particular a maximum peak inspiratory flow, PIF, achievable by the subject.

5. The method of claim 4, further comprising
    a. signaling the subject to fully exhale and subsequently inhale at maximum inhalation rate;
    b. determining whether the subject did at least approximately exhale fully and subsequently did inhale at least approximately at maximum inhalation rate;

c. if an outcome from step b) is positive, proceed with the steps of claim 3a) and b), preferably after and/or while signaling the subject to exhale;
d. if an outcome from step b) is negative, continue with step a) above; preferably after an interval; and/or preferably before and/or without carrying out steps of claims 1 and 3.

6. The method of claim 5, further comprising:
if the outcome from step b) of claim 5 is positive, switching a flow path for exhaled air before proceeding to the steps of according to claim 3a) and 3b).

7. The method of claim 5 or claim 6, further comprising:
if the outcome from step b) of claim 5 is positive, signaling the subject or an assisting person or a health care professional to switch a flow path for exhaled air before exhaling, in particular prior to proceeding to the steps according to claim 3a) and 3b).

8. An apparatus for obtaining a sample from a human or animal subject, the apparatus comprising
a. a first conduit (10) for receiving air (9) exhaled by the subject;
b. a first flowmeter (101a, 101b) provided in the first conduit;
c. a condensation vessel (3);
d. cooling means for cooling the condensation vessel;
e. a closure (1) for closing, and in particular hermetically sealing, the condensation vessel;
f. valve means (4) provided in, in particular fluidly connected with, the first conduit configured to selectively
i. channel exhaled air into the condensation vessel and out of the condensation vessel into an environment.

9. The apparatus according to claim 8, further comprising
a. a plunger (6) having a funnel, in particular an at least essentially funnel-shaped washer (61), provided on a first or distal end of said plunger (6);
b. said plunger configured to be inserted into the condensation vessel (3) through an opening (30) of said condensation vessel,
c. wherein the funnel, in particular an outer circumference of a filler opening of the funnel, is configured to wipe an inner surface (311) of the condensation

vessel, in particular of an elongate middle section (31) thereof, when being advanced into said condensation vessel.

10. The apparatus according to claim 9, wherein a channel (63) is provided in the plunger (6), said channel preferably extending through the plunger in a longitudinal direction, and configured to receive liquid collected by the funnel, in particular liquid inserted and/or flowing into the funnel's filler opening.

11. The apparatus according to one of claims 9 or 10, wherein the funnel is connected to and/or provided at a first end of the channel (63), and wherein a sample storage vial (8) may be connected to, in particular fluidly coupled to, a second end of the channel, so that the channel will direct liquid collected by the funnel, in particular liquid inserted and/or flowing into the funnel's filler opening, into the sample storage vial (8).

12. The apparatus according to one of claims 8 to 11, further comprising a receptacle (2) for the condensation vessel (3), wherein the cooling means are, in particular, configured to cool the receptacle.

13. The apparatus according to one of claims 8 to 12, wherein the first conduit (10) is further configured to channel air for aspiration to the subject.

14. The apparatus according to one of claims 8 to 13, further comprising
    a. a second conduit configured to channel air for aspiration to the subject; and
    b. a second flowmeter provided in the second conduit.

15. The apparatus according to one of claims 8 to 14, further comprising
    a. a port (11) for connecting the condensation vessel (3) to the first conduit (10), preferably in a gas-tight manner;
    b. valve means (4) for selectively channeling
        i. a flow of gas from the first conduit into the condensation vessel and back into the first conduit;
        ii. along the first conduit without entering the condensation vessel.

16. A sample collection unit for collecting, handling and storing a sample obtained from a human or animal subject, comprising

a. a vessel (3) for collecting a liquid sample, in particular a condensation vessel, for liquefying humidity contained in exhaled air;
b. a plunger (6) having a funnel, in particular an at least essentially funnel-shaped washer (61), provided on a first or distal end of said plunger (6);
c. said plunger configured to be inserted into the vessel (3) through an opening (30) of said vessel;
d. wherein the funnel, in particular an outer circumference of a filler opening of the funnel, is configured to wipe an inner surface (311) of the vessel, in particular of an elongate middle section (31) thereof, when being advanced into said vessel.

17. The sample collection unit according to claim 16, wherein a channel (63) is provided in the plunger (6), said channel preferably extending through the plunger in a longitudinal direction, and configured to receive liquid collected by the funnel, in particular liquid inserted and/or flowing into the funnel's filler opening.

18. The sample collection unit according to one of claims 16 or 17, wherein the funnel is connected to and/or provided at a first end of the channel (63), and wherein a sample storage vial (8) may be connected to, in particular fluidly coupled to, a second end of the channel, so that the channel will direct liquid collected by the funnel, in particular liquid inserted and/or flowing into the funnel's filler opening, into the sample storage vial (8).

Abstract

A method for detecting biomarkers in air exhaled by a human or animal subject, the method comprises the steps of

a. sampling, in particular collecting, air exhaled by the subject to obtain a sample;
b. subjecting the sample to biochemical analysis, in particular PCR (polymerase chain reaction), mass spectroscopy, chromatography, or magnetic resonance spectroscopy to detect a presence or absence of biomarkers in the exhaled air.

(Fig. 1)

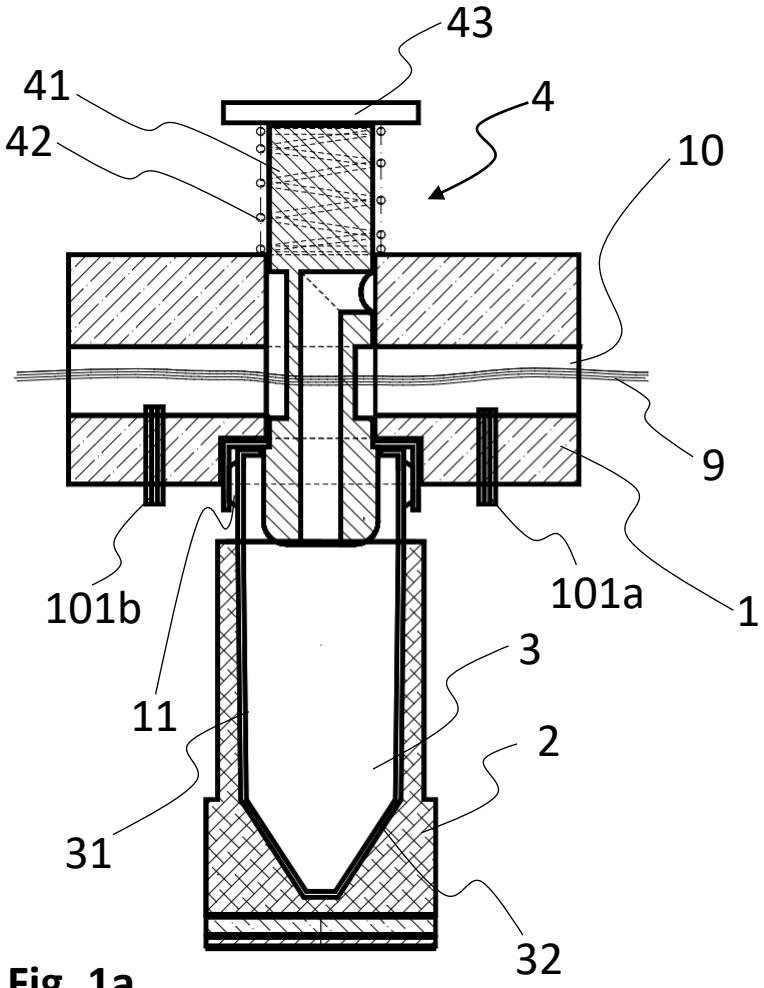

Fig. 1a

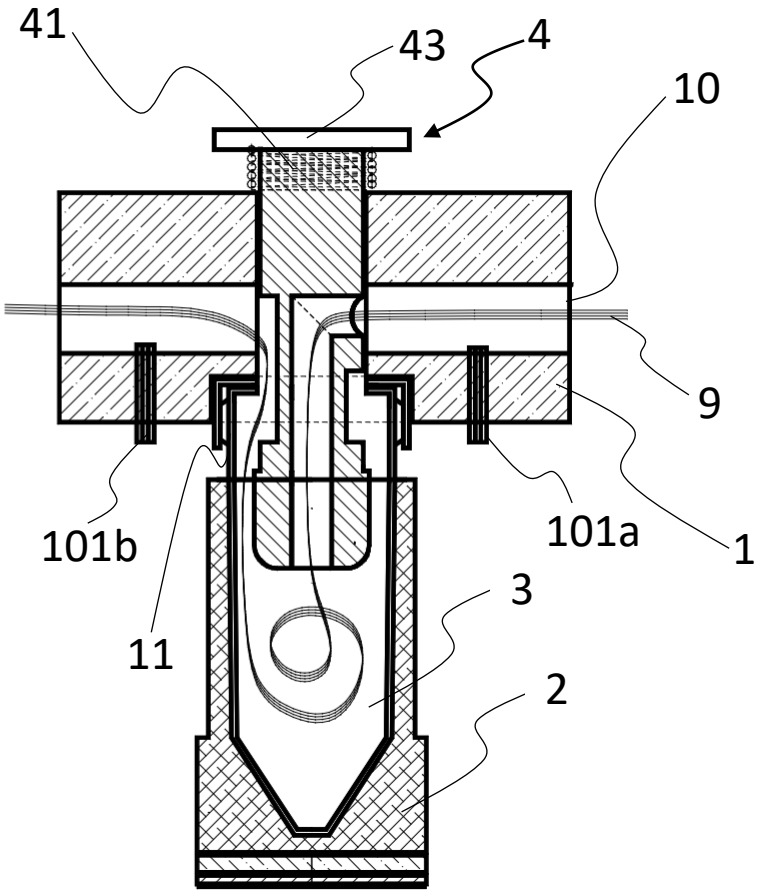

Fig. 1b

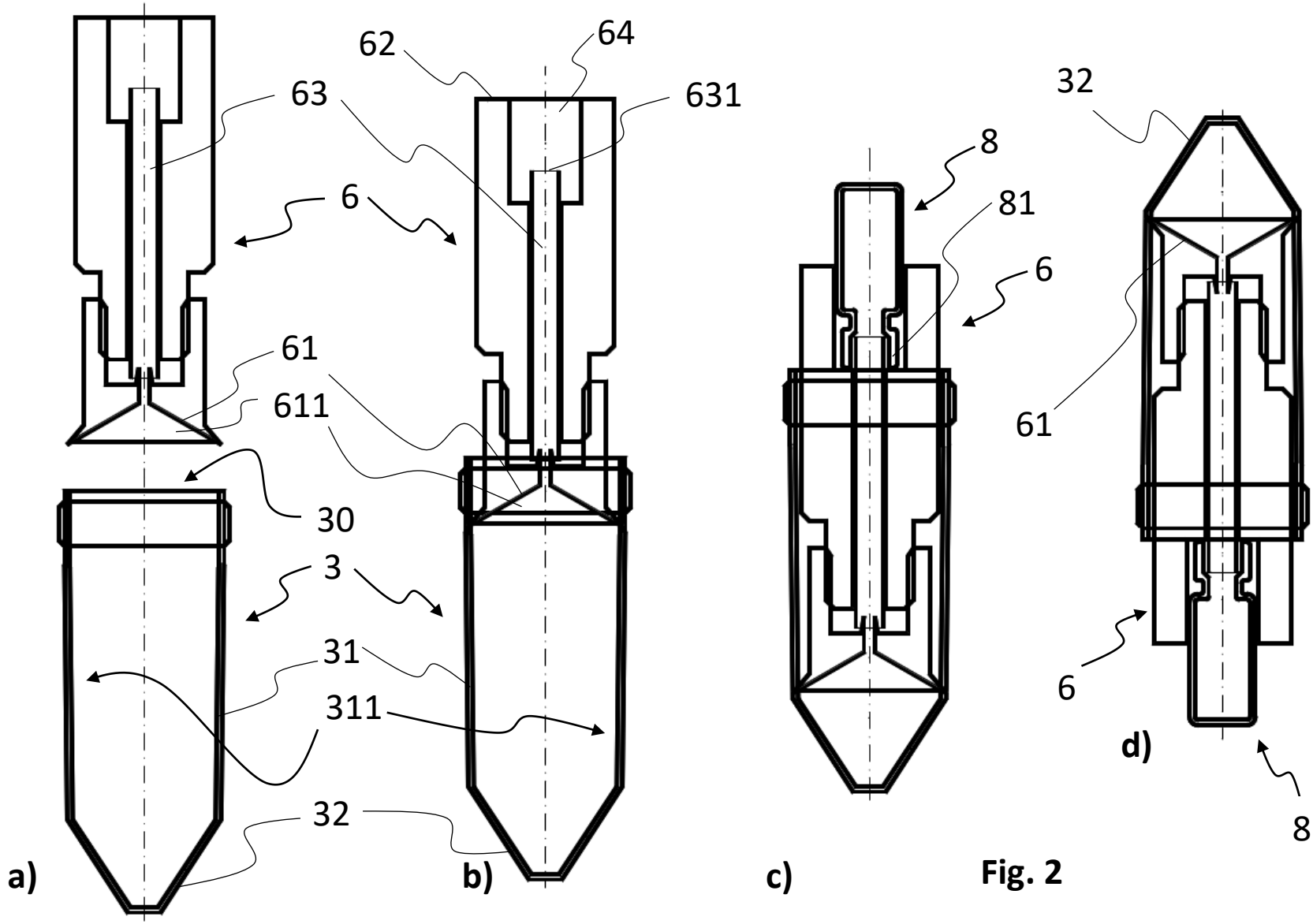

Fig. 2